Connexin 43 mediates the tangential to radial migratory switch in ventrally derived cortical interneurons.

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Authors: Laura A B Elias, Mark Turmaine, John G Parnavelas, Arnold R Kriegstein

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Scientific Abstract:
The adult cerebral cortex is composed of excitatory and inhibitory neurons that arise from progenitor cells in disparate proliferative regions in the developing brain and follow different migratory paths. Excitatory pyramidal neurons originate near the ventricle and migrate radially to their position in the cortical plate along radial glial fibers. On the other hand, inhibitory interneurons arise in the ventral telencephalon and migrate tangentially to enter the developing cortex before migrating radially to reach their correct laminar position. Gap junction adhesion has been shown to play an important mechanistic role in the radial migration of excitatory neurons. We asked whether a similar mechanism governs the tangential or radial migration of inhibitory interneurons. Using short hairpin RNA knockdown of Connexin 43 (Cx43) and Cx26 together with rescue experiments, we found that gap junctions are dispensable for the tangential migration of interneurons, but that Cx43 plays a role in the switch from tangential to radial migration that allows interneurons to enter the cortical plate and find their correct laminar position. Moreover this action is dependent on the adhesive properties and the C terminus of Cx43 but not the Cx43 channel. Thus, the radial phase of interneuron migration resembles that of excitatory neuron migration in terms of dependence on Cx43 adhesion. Furthermore, gap junctions between migrating interneurons and radial processes were observed by electron microscopy. These findings provide mechanistic and structural support for a gap junction-mediated interaction between migrating interneurons and radial glia during the switch from tangential to radial migration.